THE ASSISTANT SECRETARY OF DEFENSE

WASHINGTON, D. C. 20301-1200

HEALTH AFFAIRS

MAR 3 0 2005

The Honorable John W. Warner
Chairman, Committee on Armed Services
United States Senate
Washington, DC 20510-6050

Dear Mr. Chairman:

The enclosed report responds to the requirement contained in the Fiscal Year (FY) 2005 Department of Defense Appropriations Act Conference Report 108-622. The report was prepared by the United States Army Medical Research and Materiel Command (USAMRMC), which executes this program for the Assistant Secretary of Defense for Health Affairs. The Peer Reviewed Medical Research Program (PRMRP) was established by Congress in FY 99 to fund medical research projects that have direct relevance to military health. This report provides the PRMRP status through FY 05.

The PRMRP continues to fulfill Congressional intent by funding research of clear scientific merit with direct relevance to the health of the warfighter and the military family, as well as the American public. The FY 1999-2004 PRMRP Congressional appropriation total was $244.5 million and has provided funding for 155 projects in more than 100 topic areas. Many of the projects funded by the PRMRP have begun to yield combat health support technologies and products in the areas of Combat Casualty Care, Military Infectious Diseases, Military Operational Medicine, and Medical Chemical and Biological Defense, thus complementing the current USAMRMC core priorities. The FY 05 PRMRP is underway and is expected to continue attracting exciting research and technology development.

Thank you for your continued support of the Military Health System.

Sincerely,

William Winkenwerder, Jr., MD

Enclosure:
As stated

cc: Senator Carl Levin

REPORT TO THE US CONGRESS

PEER REVIEWED MEDICAL RESEARCH PROGRAM

March 1, 2005

Peer Reviewed Medical Research Program

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PURPOSE OF REPORT

This report provides the status of the US Army Medical Research and Materiel Command (USAMRMC) Peer Reviewed Medical Research Program (PRMRP), formerly called the Defense Health Research Program (fiscal years 1999-2000 [FY99-00]). The PRMRP was established by Congress in FY99 to fund medical research projects that have direct relevance to military health. This report provides the PRMRP status through FY05.

EXECUTIVE SUMMARY

INTRODUCTION

The Peer Reviewed Medical Research Program (PRMRP), which was originally titled Defense Health Research Program (fiscal years 1999-2000 [FY99-00]), was created by Congress in FY99 to provide support for military health-related research of clear scientific merit. The US Army Medical Research and Materiel Command (USAMRMC) is the Executive Agent for the PRMRP. The PRMRP is managed by the USAMRMC Office of the Congressionally Directed Medical Research Programs (CDMRP). The FY99-04 PRMRP congressional appropriation total was $244.5 million (M); a diverse portfolio consisting of 155 projects has been supported. The program was continued through FY05 with total appropriations to date of $294.5 M (FY99-05). Proposals are solicited via a supplement to the USAMRMC Broad Agency Announcement and undergo scientific (peer) and programmatic reviews. Proposals that most effectively address the unique focus and goals of the PRMRP are recommended for funding to the Commanding General (CG), USAMRMC by a Joint Programmatic Review Panel (JPRP). Following approval by the CG, USAMRMC, the US Army Medical Research Acquisition Activity then negotiates awards.

FY05

In FY05 $50M was appropriated to the PRMRP. The USAMRMC received funds for the PRMRP in October 2004. Twenty-one topic areas were recommended by Congress, including Acellular Human Tissue Matrix Research, Amyotrophic Lateral Sclerosis, Alcoholism Research, Anti-radiation Drug Development, Autism, Autoimmune Diseases such as Scleroderma and Sjogren's Syndrome, Blood-Related Cancer Research, Childhood Asthma, Chronic Pain Research, Conjugate Vaccines to Prevent Shigellosis, Diabetes Research, Duchenne's Disease Research, Epilepsy Research, Interstitial Cystitis, Lupus and Lupus-Biomarker Research, Orthopaedic Extremity Trauma Research, Osteoporosis and Bone Related Diseases Research, Paget's Disease, Post-Traumatic Stress Disorder, Social Work Research, and Volume Angio CAT (VAC) Research. The Office of the Assistant Secretary of Defense for Health Affairs [(ASD(HA)] added the topic areas Lung Cancer Screening and Military Relevant Disease Management especially Acinetobacter baumannii Infections, Obesity Research, and Smoking Cessation. Proposal solicitation is under way, with a deadline for proposal receipt of March 8, 2005. Peer and programmatic review will be held in May and July 2005, respectively, with award negotiations commencing in August 2005.

FY04

The total FY04 appropriation was $50M. The USAMRMC received funds for the PRMRP in January 2004. Proposals were solicited in the following 25 topic areas: Amyotrophic Lateral Sclerosis, Alcoholism Research, Anti-Diarrhea Supplement, Blood-Related Cancer Research, Childhood Asthma, Chronic Pain Research, Epilepsy Research, Geneware Rapid Vaccine Development, Interventional Cardiovascular Magnetic Resonance Imaging Technologies, Muscle Function Research, Malaria Vaccine Initiative [SBRI], Muscular Dystrophy, Osteoporosis and Bone

Related Disease Research, Padget's [sic] Disease, Providence Cancer Research Project, Post-Traumatic Stress Disorder, Social Work Research, Interstitial Cystitis, Military Medical Informatics Research, Limb Loss and Paralysis Research, and Reserve Component Medical Training Program; Smoking Cessation, Pseudofolliculitis Barbae, Lung Cancer Screening, and Military Relevant Disease Management (especially research on Malaria, Leishmaniasis, and Wound Infections) were added by ASD(HA). Proposals were received in March 2004 and underwent peer and programmatic reviews in May and July 2004, respectively. Twenty-eight proposals were approved for funding by the CG, USAMRMC. The majority of the grants have been awarded, and the remainder will be awarded by March 2005.

FY99-03

The total FY99-03 PRMRP congressional appropriation was $194.5M. Proposals were solicited in 15, 18, 31, 25, and 28 topic areas, respectively. Following scientific peer review and programmatic review, a total of 127 proposals was approved for funding by the CG, USAMRMC. A portion of FY99 and FY01 PRMRP funds was assigned by the ASD(HA) for management outside the CDMRP. In FY99, $4M was assigned to the Brooke Army Medical Center to support a Chronic Disease Management Project focusing on congestive heart failure. Management responsibility for the project was assigned to the USAMRMC Office of Telemedicine and Advanced Technology Research Center (TATRC). In FY01, $10M was assigned to the Naval Health Research Center to support the Department of Defense (DOD) portion of the Leadership and Investment in Fighting an Epidemic (LIFE) Initiative. Management responsibility for this project was assigned to the Navy Bureau of Medicine and Surgery (BUMED).

PROGRESS/ACCOMPLISHMENTS

A number of the FY99-03 funded projects, those managed by the CDMRP and those managed by TATRC and BUMED, have already produced interesting research outcomes relevant to military health issues. These projects range from basic research to technology development and cover more than 100 topic areas, including: Acute Lung Injury, Childhood Asthma, Smoking Cessation, Alcohol Abuse Prevention, and Military Relevant Disease Management. Examples of research outcomes include a systematic way of delivering antioxidants and clot-dissolving enzymes into the lung to prevent inflammation; creation of a video-based tobacco cessation intervention aimed at decreasing tobacco use in the military; development of a Closed-Loop Frozen Blood Processing model unit (the manufacturable unit will provide the Armed Forces a more practical choice between fresh packed red blood cells and a frozen red cell alternative); development of an improved dengue fever vaccine; design of an Internet-based, in-home asthma monitoring system for children; development of an improved method for improved healing of war wounds; a prototype miniature surgical robot; development of a food-based antidiarrheal supplement; creation of a field-deployable assay system for detecting biological toxins; and development of a self-operated, portable, low irradiance treatment device for pseudofolliculitis barbae, a significant dermatologic disease in the US Army.

SUMMARY

The PRMRP continues to fulfill congressional intent by funding research of clear scientific merit with direct relevance to the health of the warfighter and the military family, as well as the American public. The FY99-04 PRMRP congressional appropriation total was $244.5M and has provided funding for 155 projects in more than 100 topic areas. Many of the projects funded by the PRMRP have begun to yield combat health support technologies and products in the areas of Combat Casualty Care, Military Infectious Diseases, Military Operational Medicine, and Medical Chemical and Biological Defense, thus complementing the current USAMRMC Core priorities. The FY05 PRMRP is under way and is expected to continue attracting exciting research and technology development.

FISCAL YEAR 1999-2005 PEER REVIEWED MEDICAL RESEARCH PROGRAM

I. INTRODUCTION

The Peer Reviewed Medical Research Program (PRMRP) was created by Congress in fiscal year 1999 (FY99) to provide support for military health-related research of clear scientific merit. The program was continued through FY05 with total appropriations of $294.5 million (M) (FY99-05) via Defense Health Programs; Research, Development, Test and Evaluation (DHP, RDT&E). The US Army Medical Research and Materiel Command (USAMRMC) was selected by the Office of the Assistant Secretary of Defense for Health Affairs [(ASD(HA)] as Executive Agent for this program through Joint Services coordination and the specific recommendation of the Armed Services Biomedical Research Evaluation and Management Committee. The PRMRP is managed through the USAMRMC Office of the Congressionally Directed Medical Research Programs (CDMRP). The administrative process includes establishing a yearly execution strategy and programmatic priorities to include scientific merit and military relevance. The management strategy is established by an interagency Joint Programmatic Review Panel (JPRP), which consists of representatives from the Army, Air Force, Navy, Marine Corps, ASD(HA), and Departments of Veterans Affairs and Health and Human Services. Proposals for each year's program are solicited via a supplement to the USAMRMC Broad Agency Announcement. Following receipt, proposals undergo scientific merit review (peer review), conducted by external scientific and clinical experts, as well as programmatic review conducted by the JPRP. The JPRP, through defined programmatic priorities, recommends proposals that most effectively address the unique focus and goals of the PRMRP for funding to the Commanding General (CG), USAMRMC (who holds final approval authority). Following approval by the CG, USAMRMC, awards are negotiated by the US Army Medical Research Acquisition Activity.

II. PROGRAM OVERVIEW

FY05

In FY05, $50M was appropriated to the PRMRP. The USAMRMC received funds for the PRMRP in October 2004. Twenty-one topic areas were recommended by Congress, including Acellular Human Tissue Matrix Research, Amyotrophic Lateral Sclerosis, Alcoholism Research, Anti-radiation Drug Development, Autism, Autoimmune Diseases such as Scleroderma and Sjogren's Syndrome, Blood-Related Cancer Research, Childhood Asthma, Chronic Pain Research, Conjugate Vaccines to Prevent Shigellosis, Diabetes Research, Duchenne's Disease Research, Epilepsy Research, Interstitial Cystitis, Lupus and Lupus-Biomarker Research, Orthopaedic Extremity Trauma Research, Osteoporosis and Bone Related Diseases Research, Paget's Disease, Post-Traumatic Stress Disorder, Social Work Research, and Volume Angio CAT (VAC) Research. The ASD(HA) added the topic areas Lung Cancer Screening and Military Relevant Disease Management especially Acinetobacter baumannii Infections, Obesity Research, and Smoking Cessation. Proposal solicitation is under way, with a proposal receipt deadline of March 8, 2005. Peer review by an external panel of scientists will be held in May 2005. Programmatic review will

be conducted by the JPRP in July 2005. Award negotiations will begin in August 2005. All awards will be managed for scientific progress as well as for regulatory and budgetary requirements.

FY04

In FY04, $50M was appropriated to the PRMRP. The USAMRMC received funds in January 2004. The conferees directed that research efforts could include Amyotrophic Lateral Sclerosis, Alcoholism Research, Anti-Diarrhea Supplement, Blood-Related Cancer Research, Childhood Asthma, Chronic Pain Research, Epilepsy Research, Geneware Rapid Vaccine Development, Interventional Cardiovascular Magnetic Resonance Imaging Technologies, Muscle Function Research, Malaria Vaccine Initiative [SBRI], Muscular Dystrophy, Osteoporosis and Bone Related Disease Research, Padget's [sic] Disease, Providence Cancer Research Project, Post-Traumatic Stress Disorder, Social Work Research, Interstitial Cystitis, Military Medical Informatics Research, Limb Loss and Paralysis Research, and Reserve Component Medical Training Program. Proposals were solicited in these 21 topic areas and in four additional topic areas including: Smoking Cessation, Pseudofolliculitis Barbae, Lung Cancer Screening, and Military Relevant Disease Management (especially research on Malaria, Leishmaniasis, and Wound Infections). These four topic areas were added by ASD(HA). Twenty-eight proposals were approved by the CG, USAMRMC. The majority of the grants have been awarded, and the remainder will be awarded by March 2005. Detailed funding information (including congressional appropriation and associated withholds, as well as proposals received and funded by topic area and institution) is provided in Tables I and II.

Table I: FY04 PRMRP Funding Outcomes by Topic Area

Topic Area	# Proposals Received	# Recommended for Funding	Organization	Proposal Title
Alcoholism Research	15	1	Oregon State University	Alcohol Impaired Bone Healing: Mechanisms and Countermeasures
Amyotrophic Lateral Sclerosis	30	2	Johns Hopkins University	Function of Prostoglandin Receptors in Models of ALS
			Harvard University	Prospective Study of ALS Mortality among World War II, Korea, and Vietnam Veterans
Anti-Diarrhea Supplement	0	0		
Blood-Related Cancer Research	25	2	University of Pennsylvania	PECAM-1 and Angiogenesis
			Mount Sinai School of Medicine	Tracking the Fate of the Aberrant Clone in Patients with the Myelodysplastic Syndrome: The Influence of Treatment on Clonal Selection and Function

Topic Area	# Proposals Received	# Recommended for Funding	Organization	Proposal Title
Childhood Asthma	8	1	Emory University	Prenatal Exposure to Nicotine and Childhood Asthma: Role of Nicotinic Acetylcholine Receptors
Chronic Pain Research	9	1	University of Texas	Use of PC-NSAIDs in Chronic Pain
Epilepsy	11	1	University of Pennsylvania	Preventing Epilepsy after Traumatic Brain Injury
Geneware Rapid Vaccine Development	1	1	Brentwood Biomedical Research Institute	Bacteroids Fragilis OMP A: Utility as a Live Vaccine Vector for Biodefense Agents
Interstitial Cystitis Research	4	0		
Interventional Cardiovascular Magnetic Resonance Imaging Technologies	1	0		
Limb Loss and Paralysis Research	16	2	Boston VA Research Institute, Inc.	Autologous Marrow Derived Stem Cell-Seeded Gene-Supplemented Collagen Scaffolds for Spinal Cord
			Case Western Reserve University	A Hybrid Neuroprosthesis for Mobility after Paralysis from Spinal Cord Injury
Lung Cancer Screening*	5	1	University of Pittsburgh	Development and Evaluation of Stereographic Display for Lung Cancer Screening
Malaria Vaccine Initiative [SBRI]	1	1	Seattle Biomedical Research Institute	Antigens for a Vaccine to Prevent Severe Malaria
Military Medical Informatics Research	8	0		

* Topic Area added by ASD(HA)

Topic Area	# Proposals Received	# Recommended for Funding	Organization	Proposal Title
Military Relevant Disease Management (especially research on Malaria, Leishmaniasis, and Wound Infections)*	80	7	IQuum, Inc.	Nucleic Acid Testing Device for the Use at Battalion Aid Stations
			Henry M. Jackson Foundation (Walter Reed Army Medical Center)	Progression of Coronary Artery Calcium Progression on EBCT Scanning in Active Military Personnel: Role of Ethnicity and the Metabolic Syndrome
			Albert Einstein College of Medicine	Evaluation of Purine Salvage as a Chemotherapeutic Target in the Plasmodium Yoelii Rodent Malaria
			Brentwood Biomedical Research Institute	Rapid Identification of Key Pathogens in Wound Infection by Molecular Means
			New York Medical College	Control of Spinal Cord Injury by Stereotactic X-Irradiation
			Henry M. Jackson Foundation (Naval Medical Research Center)	Development of Recombinant Adenoviral-Based Vaccines against Malaria
			University of Alabama at Birmingham	Pharmacologic Intervention to Reduce Morbidity and Mortality following Trauma, Hemorrhage, Burn, Fracture, and Sepsis
Muscle Function Research	20	2	University of Iowa	Muscle Cell Membrane Maintenance and Repair
			University of Illinois Chicago	Enhancement of Skeletal Muscle Repair by the Urokinase-Type Plasminogen Activator System
Muscular Dystrophy	5	0		
Osteoporosis and Bone Related Disease Research	35	3	Oregon Health and Science University	Enhanced Androgen Signaling with Androgen Receptor Overexpression in the Osteoblast Lineage Controls Skeletal Turnover, Matrix Quality and Bone Architecture
			Southwest Research Institute	Targeted Therapies for Myeloma and Metastatic Bone Cancers
			University of Michigan	Identification of RNA Binding Proteins That Effect IL-6 mRNA Stability: Development of Novel Targets for Management of Inflammatory Bone Diseases

* Topic Area added by ASD(HA)

Topic Area	# Proposals Received	# Recommended for Funding	Organization	Proposal Title
Paget's Disease	0	0		
Post-Traumatic Stress Disorder	21	1	Brown University	Treatment of PTSD-Related Anger in Troops Returning from Hazardous Deployments
Pseudofolliculitis Barbae*	0	0		
Reserve Component Medical Training	3	1	University of Miami School of Medicine	Medical Reservist Team Training Program: Achieving Optimal Outcomes and Improving Team Performance Using Simulation-Based Teamwork and Safety Interventions
Providence Cancer Research Project	1	0		
Smoking Cessation*	6	1	Nova Southern University	Facilitating Smoking Cessation and Preventing Relapse in Primary Care: Minimizing Weight Gain by Reducing Alcohol Consumption
Social Work Research	3	0		
Total	308	28		

* Topic Area added by OASD(HA)

Table II: FY04 PRMRP Appropriation, Withholds, and Estimated Research and Management Costs

FY04 Appropriation	$50,000,000
Less: Small Business Innovation Research	($1,250,000)
Amount Released to USAMRMC	$48,750,000
Less: Estimated USAMRMC Overhead and Management Costs	($6,190,000)
Estimated Research	$42,560,000

FY99-03

The FY99-03 PRMRP congressional appropriations totaled $194.5M. Proposals were solicited in 15, 18, 31, 25, and 28 topic areas, respectively. A total of 127 proposals that most effectively addressed the unique focus and goals of the PRMRP was approved for funding by the CG,

USAMRMC. Detailed funding information including topic areas offered, proposals received, and awards made is provided by fiscal year in Appendix I.

Fourteen million dollars of the $194.5M appropriated to the PRMRP was managed outside the CDMRP. Four million dollars of the FY99 PRMRP appropriation was assigned to the Brooke Army Medical Center by the ASD(HA) to support a Chronic Disease Management Project, focusing on Congestive Heart Failure. Management responsibility was assigned to the USAMRMC Office of Telemedicine and Advanced Technology Research Center in FY01. Research accomplishments for this project are provided in Appendix II.

Ten million dollars was assigned to the Naval Health Research Center and managed by the Navy Bureau of Medicine and Surgery to support the Department of Defense (DOD) portion of the Leadership and Investment in Fighting an Epidemic (LIFE) Initiative from the FY01 PRMRP appropriation. Research accomplishments for this project are provided in Appendix III.

III. ACCOMPLISHMENTS

PRMRP Response to Urgent Needs

The FY99-03 PRMRP-funded projects are yielding valuable research outcomes and the development and deployment of technologies that are relevant to military health. The flexibility of the PRMRP allows a quick response to new and changing priorities in military health. For example, the importance of understanding and treating acute lung injury has been highlighted by the current US involvement in military conflict in Afghanistan and Iraq, as well as increased likelihood of chemical weapons attacks. Childhood asthma is increasing in incidence in all populations, but its large financial and human cost to the military is a serious drain on resources.

Acute Lung Injury/Acute Respiratory Distress Syndrome: Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are life-threatening conditions in which inflammation of the lungs and accumulation of fluid in the air sacs (alveoli) lead to low blood oxygen levels. ALI or ARDS can result from severe traumatic injury, hemorrhage, severe burns, and inhalation of smoke or chemicals, and mortality rates are 20%-30%. The prevalence of ARDS appears to be increasing in modern combat, and it is also likely to be a major outcome of a chemical weapons attack on military or civilian personnel. Use of a lung-protective mechanical ventilator is the best available treatment, but this requires sensitive equipment and close supervision and is not appropriate for battlefield or mass casualty situations.

Dr. Leopoldo Cancio at the US Army Institute of Surgical Research is exploring the use of an intravenous membrane oxygenator implanted directly in the vena cava to provide improved oxygen/carbon dioxide exchange in the blood without a large external pump, using sheep as a model. An alternative approach is being taken by Dr. Vladimir Muzykantov of the Pennsylvania State University. Deposition of fibrin and blood clots in the lungs and oxidative stress in the lung vasculature contribute to ALI and ARDS. Delivering antioxidant and clot-dissolving enzymes directly to the lungs could help prevent the lung inflammation that leads to low blood oxygen levels. These enzymes can be directed to the lungs by linking them to antibodies targeting the surface of

the endothelial cells such as those lining the lungs. Dr. Muzykantov is currently testing antibody delivery systems in mice, with plans to advance to larger animal models.

Childhood Asthma: Asthma is the leading cause of chronic disease in childhood and has a marked impact on military families. Management of childhood asthma requires effective medical therapy, adherence to the medical therapy, and patient education and monitoring. Estimates about the prevalence of asthma among children and adolescents under the age of 18 range up to 7%. Compared to their peers, children with asthma missed an additional 10.1 million days of school, had 12.9 million more contacts with physicians, and were hospitalized 200,000 more times in 1988. The estimated economic impact of asthma in the United States exceeds $2.0 billion per year.

Dr. Shibata and colleagues at Florida Atlantic University have identified a promising preventive treatment for asthma. Oral administration of tiny particles of chitin, a naturally occurring polymer from shellfish, reduced the allergic response in mice allergic to ragweed. The treatment decreased typical immune responses seen in both allergies and asthma, such as serum levels of immunoglobulin E and eosinophils in the lungs. Dr. Shibata's group is studying the molecular basis of chitin's effect to lay the groundwork for possible clinical trials of chitin in humans.

Researchers at the Tripler Army Medical Center designed an Internet-based, in-home asthma monitoring system for children. In addition to attending a pediatric asthma clinic at regular intervals, participants are provided with home computers and Internet access and they are monitored over the Internet. Therapeutic monitoring includes digital videos of patients using their controller medication inhaler and videos of peak flow meter use. Videos are submitted electronically twice a week by using in-home telemonitoring with store-and-forward technology. In a small pilot test, participants improved their inhaler use technique and hospital visits were reduced.
COL Charles Callahan and colleagues are conducting a large scale trial of the Internet-based asthma monitoring system, comparing patients' quality of life, utilization of services, rescue-therapy use, symptom control, and retention of asthma knowledge in groups using the Internet system or a traditional office-based education system. The technology could allow military families of children afflicted by asthma to be monitored at a distance from medical centers or clinics, but still benefit from the close care of asthma experts, reducing the psychological burden as well as the costs associated with such care.

PRMRP Coordination with USAMRMC Core Mission

The PRMRP continues to support research and technology development in all areas affecting the military, including wellness and fitness, infectious disease research, military operational medicine, and combat casualty care. The PRMRP projects complement the core research and development areas of the USAMRMC Research Area Directorates (RADs). The PRMRP staff coordinates with the RADs to avoid overlap and duplication and to help bring PRMRP-funded technologies to deployment. Several PRMRP-funded projects are in active product development.

Wellness and Fitness Research

Smoking Cessation: The prevalence of tobacco use is much higher among US military personnel than among the civilian population. Dr. Linda Trent and colleagues at the Naval Health Research Center are developing and testing a self-contained video-based tobacco cessation intervention aimed

at addressing this problem. Thus far, Dr. Trent has completed baseline data collection and video intervention of more than 12,000 US Marine Corps (USMC) participants. Her data indicate a 49% prevalence of smoking among USMC recruits, a 9% higher daily use of tobacco as compared with the civilian cohort, and a prevalence of smokeless tobacco use six times higher than among the civilian cohort. An educational approach specifically for smokeless tobacco cessation is being applied by Dr. Herbert Severson at the Oregon Research Institute. A brief tobacco cessation intervention can easily be incorporated into a dental examination and may be more effective for smokeless tobacco users than a structured group program. The treatment program incorporates proactive recruitment through motivational interviewing and has proven successful in a large study with a civilian population as well as a pilot study with Air Force personnel. Eleven dental clinics at nine military bases have begun enrolling subjects in the program.

Alcohol Abuse: Alcohol misuse in the military is costly and has been identified as an important factor in aggressive behavior in humans. Therefore, the military is attempting to deglamorize alcohol use and reduce alcohol abuse among its military personnel. Andrea Allan and colleagues at the University of New Mexico are examining the impact of serotonin receptor 3 (5HT3) overexpression on alcohol preference, natural aggressive behavior, and alcohol-heightened behavior. Previous studies indicating that the 5HT3 receptor system mediates alcohol consumption and the subjective effects of alcohol are supported by Dr. Allan's work. Results of studies in mice indicate that overexpression of 5HT3 both reduces alcohol preference and decreases the display of aggressive behavior. An important outcome of this work is the development of a mouse model for fetal alcohol exposure.

Infectious Disease Research

Malaria: Treatment of malaria is becoming increasingly difficult because of the emergence of multidrug-resistant strains of *Plasmodium falciparum*, causative agent of the most severe form of the disease. As a result, there is a pressing need to develop novel antimalarial agents. Dr. Michael Riscoe of the Portland, Oregon Veterans Affairs Medical Center has shown that naturally occurring hydroxyxanthones appear to disrupt the stage in which malaria parasites live in human blood cells by interfering with the parasites' ability to dispose of toxic waste products. Dr. Riscoe has synthesized two hydroxyxanthone analogues and performed preliminary studies in a mouse malaria model. The drugs were nontoxic to the mice and reduced the parasitemia of malaria by 90%.

Dengue: Dengue Fever is a mosquito-born viral disease endemic in tropical regions around the world. Dengue vaccines in clinical trials use attenuated viruses. DNA vaccines have the potential to give a more robust immune response, but have shown only partial protection to live virus challenge in mice and primates. Dr. Kevin Porter and colleagues at the Naval Medical Research Center are using mice as a model to explore the use of tetanus toxoid, aluminum phosphate, and monoclonal antibodies as adjuvants to improve the efficacy of the DEN-1 and DEN-2 DNA vaccines.

Diarrhea: Diarrhea is a significant health threat for military and civilian travelers to developing countries. Incidence rates as high as 50% occur where food and water sanitation is poor. The military requirement for solutions in this area is becoming more acute. Since the inception of the war on terrorism, the global commitment of US fighting forces has been increasingly concentrated in developing areas of the world. Rehydration and antibiotic treatment are the cornerstones of disease management, but even with early institution of appropriate therapy, diarrheal diseases exact

a cost in terms of lost duty and effectiveness. There is no licensed drug or biologic that provides a safe, effective mode of prevention, leaving an important deficiency in military and travel medicine. CAPT Stephen Savarino at the Naval Medical Research Center in collaboration with Johns Hopkins University is developing bovine milk immunoglobulins (BIgG) as a supplement with activity against enterotoxigenic *Escherichia coli*, the predominant cause of traveler's diarrhea. **This investigational treatment has shown proof of principle as a safe, food-based anti-diarrheal supplement and is slated to begin clinical trials in 2005.**

Military Operational Medicine Research

Remote surgical capability (i.e., telesurgery) could be used in the battlefield to improve the care of wounded military personnel in the critical hour after injury. Such technology also would benefit civilian medical care in rural areas. Dr. Blake Hannaford of the University of Washington is developing a miniature surgical robot system and has completed a prototype based on kinematic analysis of surgical performance. The prototype allowed maximal dexterity throughout the surgical space and included a flexible manipulator for surgical tools. Dr. Hannaford will test the prototype robot in surgery on pigs and determine the learning curve on the robot for experienced surgeons.

Making fresh blood products available in field or remote situations is a challenge for the Armed Forces. Researchers at Mission Medical, Inc. in Fremont, California, developed a prototype automated red blood cell processing system for preparing blood for transfusions. This prototype rapidly performs the freezing, thawing, and reconstitution of whole red blood cells in a sterile closed loop system, resulting in a liquid blood product that can be refrigerated for up to 2 weeks. Under the direction of Dr. Thomas Robinson, Mission Medical will design modifications to the disposables and hardware to improve manufacturability and decrease cost, perform regulatory studies, and perform field testing at military sites to demonstrate the practicality, acceptance, and fulfillment requirements by this system.

The protection of military personnel deployed in hostile peacekeeping or combat situations depends on the early and rapid detection of biological toxins, which can be lethal at extremely low concentrations. Dr. Jeffrey Mason of the Armed Forces Institute of Pathology is developing a simple and reliable field-deployable assay system for detecting biological toxins. The goal is to achieve high specificity at concentrations of less than 250 molecules. Dr. Mason and colleagues have developed an assay system in which tiny amounts of toxins are identified by immunoassay linked to polymerase chain reaction amplification of DNA. They have achieved a sensitivity of detection of 2,500 molecules for botulinum toxoid and 3,000 molecules for tetanus toxoid.

Pseudofolliculitis barbae (PFB or shaving bumps) is an inflammatory condition of the beard area, usually observed in dark skinned men with thick, coarse hair who shave regularly. Currently available depilatories, topical creams, and so-called PFB razors do not offer a permanent definitive answer for PFB and, at best, only temporarily ameliorate the condition. PFB can impact force readiness, compromise the ability to wear close-fitting protective facial gear, and affect the soldier's quality of life. This condition is considered a significant dermatologic disease in the US Army; it affects more than 50% of African American servicemen. Laser- and lamp-based modalities that were initially developed for removal of unwanted body hair have the potential to provide a curative solution to the problem. Palomar Medical Products, Inc. is developing a self-operated, portable, low irradiance PFB treatment device that can be used by individuals without physician supervision. **Current protocols are in clinical trials at the Naval Medical Center in San Diego using a**

larger, physician operated system. Further trials are planned for smaller units using self-treatment parameters.

Combat Casualty Care Research: Impaired healing of war wounds is a serious military medical problem. Wound healing could be improved by targeting cellular growth factors to wounds. Gene therapy can deliver growth factors continuously deep within the tissue to maximally enhance healing. The potential of gene therapy has not been exploited because the technology to deliver the genes has not been successful. Dr. John Harmon and colleagues at Johns Hopkins University are using electroporation, in which an electric field passed through tissue opens small pores in cell membranes to successfully deliver DNA molecules into cells. The Johns Hopkins team used mouse models to study the effect of delivering the gene for keratinocyte growth factor (KGF) by electroporation. The technique improved the speed of closure in slow-healing wounds produced experimentally in mice. An additional benefit of this technique may be the treatment of slow wound healing in diabetics as observed in diabetic mice having KGF delivered into wounds by electroporation.

There are many medical challenges to consider for far-forward medical care to reduce mortality and morbidity associated with major battlefield wounds and injuries. In particular, trauma and hemorrhage are a leading cause of death in the US and a major concern of the military. Significant loss of blood leads to shock, a condition of inadequate organ perfusion, and tissue oxygenation, and there is the need for intelligent medical systems to guide corpsmen and combat medics in triage and resuscitation of severely injured combatants. Scientists at the University of Massachusetts Medical School in collaboration with Luxtec Corporation have developed and tested a prototype, portable sensor system based on near infrared spectroscopy to noninvasively measure tissue perfusion. This system quickly and accurately measures muscle pH, muscle oxygen tension, and hematocrit from light reflected from the palm of the hand and will guide combat medical personnel in resuscitation care and evacuation. **The prototype device and additional units are currently in ongoing clinical trials and scheduled for product delivery to the USAMRMC's Core Combat Casualty Care Research Program later in 2005 for further field testing and evaluation.**

IV. SUMMARY

The PRMRP continues to fulfill congressional intent by funding research of clear scientific merit with direct relevance to the health of the warfighter, the military family, and the American public. The FY99-05 PRMRP congressional appropriation total was $244.5M and has provided funding for 155 projects in more than 100 topic areas. Many of the projects funded by the PRMRP have begun to yield combat health support technologies and products in the areas of Combat Casualty Care, Military Infectious Diseases, Military Operational Medicine, and Medical Chemical and Biological Defense, thus complementing current USAMRMC Core priorities. The FY05 PRMRP is under way and is expected to continue attracting exciting research and technology development.

USAMRMC Point of Contact is Colonel Kenneth Bertram, 301-619-7071, Kenneth.Bertram@det.amedd.army.mil

APPENDICES

APPENDIX I – PRMRP FUNDING SUMMARIES

Table I: FY99 DHRP Funding Outcomes by Topic Area and Institution

Topic Area	Institution	Budget
Alcoholism Research	The Nathan S. Kline Institute for Psychiatric Research	$475,282
Alcoholism Research	University of New Mexico Health Sciences Center	$715,039
Alcoholism Research	Louisiana State University Health Sciences Center	$510,217
Alcoholism Research	Research Triangle Institute	$1,608,635
Alcoholism Research	University of New Mexico Health Sciences Center	$387,460
Alcoholism Research	University of Minnesota School of Medicine	$607,086
Alcoholism Research	Tripler Army Medical Center	$230,120
Chemical Weapons Treatment	Uniformed Services University of the Health Sciences	$1,283,218
Disease Management	Walter Reed Army Medical Center	$744,500
Healthcare Information Protection	University of California at San Francisco	$916,343
Lung Research	Naval Health Research Center	$425,337
Pediatric Asthma	Brooke Army Medical Center	$75,329
Pediatric Asthma	State University of New York at Buffalo	$209,778
Sleep Management	Walter Reed Army Institute of Research	$1,758,569
Sleep Management	NTI, Inc.	*$1,425,170
Smoking Cessation	University of Minnesota	$2,774,406

*Grant was funded with FY99 research dollars in the amount of $1,269,274 and FY02 research dollars in the amount of $155,896.

Table II: FY00 PRMRP Funding Outcomes by Topic Area and Institution

Topic Area	Institution	Budget
Advanced Soft Tissue Modeling	Massachusetts General Hospital	$1,968,490
Advanced Soft Tissue Modeling	Cleveland Clinic Foundation	$1,845,080
Alcohol Abuse Prevention Research	University of New Mexico	$525,212
Alcohol Abuse Prevention Research	Pacific Institute for Research and Evaluation	$964,853
Alcohol Abuse Prevention Research	University of New Mexico	$1,336,262
Alcohol Abuse Prevention Research	Johns Hopkins University, East Baltimore Campus	$1,191,816
Childhood Asthma	Tripler Army Medical Center	$1,547,400
Defense and Veterans Head	National Institutes of Health, Bethesda	*$2,405,483

Topic Area	Institution	Budget
Injury Program		
Defense and Veterans Head Injury Program	US Army Aeromedical Research Laboratory	$948,121
Dengue Fever Vaccine Research	Naval Medical Research	$439,850
Gulf War Illnesses	Wake Forest University School of Medicine	$790,884
Gulf War Illnesses	Walter Reed Army Medical Center	$445,078
Militarily Relevant Disease Management	Naval Submarine Medical Research Laboratory	**$5,826,062
Militarily Relevant Disease Management	Walter Reed Army Medical Center	$1,730,872

*Grant was funded with FY00 research dollars in the amount of $2,133,483 and FY02 research dollars in the amount of $272,000.
**Grant was funded with FY00 research dollars in the amount of $5,326,062 and FY02 research dollars in the amount of $500,000.

Table III: FY01 PRMRP Funding Outcomes by Topic Area and Institution

Topic Area	Institution	Budget
Acute Lung Injury Research	University of Arizona	$1,268,823
Acute Lung Injury Research	Johns Hopkins University	$386,236
Acute Lung Injury Research	University of Pennsylvania	$1,283,287
Acute Lung Injury Research	Northeastern University	$113,137
Acute Lung Injury Research	Atlanta Research and Education Foundation	$671,010
Acute Lung Injury Research	Johns Hopkins University	*$2,013,226
Alcohol Abuse Prevention Research	University of Illinois at Chicago	$1,042,703
Arthropod Transmitted Infectious Disease	University of Connecticut Health Center	$894,632
Arthropod Transmitted Infectious Disease	Albert Einstein College of Medicine	$1,053,074
Arthropod Transmitted Infectious Disease	Albert Einstein College of Medicine	$1,185,539
Arthropod Transmitted Infectious Disease	University of Texas Medical Branch	$1,284,529
Biological Hazard Detection System/Bio-sensor Microchip	American Registry of Pathology	$382,691
Childhood Asthma	West Virginia University Research Corporation	$898,623
Childhood Asthma	Lackland Air Force Base	$652,675
Childhood Asthma	University of Minnesota	$1,672,392
Digital Mammography Imaging	University of Michigan	$1,717,673
Fungi Free	Ganeden Biotech, Inc.	$319,745

Topic Area	Institution	Budget
Gulf War Illnesses	Veterans Affairs Medical Center	$1,689,945
Gulf War Illnesses	Armed Forces Radiobiology Research Institute	$382,829
Gulf War Illnesses	Naval Health Research Center	$696,627
Laser Eye Injury/Eye Cancer Research and Treatment	Brooks Air Force Base	$756,250
Laser Eye Injury/Eye Cancer Research and Treatment	Johns Hopkins University	$549,638
Medical Surgery Technology	University of Washington	$1,198,256
Militarily Relevant Disease Management	University of Miami School of Medicine	$739,056
Militarily Relevant Disease Management	Johns Hopkins University	$243,452
Militarily Relevant Disease Management	Naval Health Research Center/ University of Ottawa	$1,190,116
Militarily Relevant Disease Management	University of Illinois College of Medicine	$965,931
Militarily Relevant Disease Management	Walter Reed Army Institute of Research	$191,715
Militarily Relevant Disease Management	Tripler Army Medical Center	$1,817,797
Molecular Biology for Cancer Research	Thomas Jefferson University	$965,282
Molecular Biology for Cancer Research	Walter Reed Army Medical Center	$734,261
Molecular Biology for Cancer Research	Thomas Jefferson University	$802,398
Obesity Related Disease Prevention (esp. for minorities)	Baylor College of Medicine	$964,601
Remote Emergency Medicine Ultrasound	GE Corporate Research and Development	$1,992,742
Sleep Management	Veterans Medical Research Foundation	$1,701,135
Smoking Cessation	Oregon Research Institute	$1,949,634
Smoking Cessation	Naval Health Research Center	$465,267

* Grant was funded with FY01 research dollars in the amount of $645,851 and FY02 research dollars in the amount of $1,367,375.

Table IV: FY02 PRMRP Funding Outcomes by Topic Area and Institution

Topic Area	Institution	Budget
Acute Lung Injury Research	US Army Institute of Surgical Research	$1,980,400
Chemo-Preventative Approaches to Smoking Related Illness	University of Arizona	$1,261,963
Childhood Asthma	East Carolina University	$920,999
Closed Loop Frozen Blood Processing Systems	Mission Medical, Inc.	$1,499,916
Dengue Fever Vaccine	Naval Medical Research Center	$1,079,876
High Risk Infectious Disease	UCLA School of Medicine	$1,850,112
High Risk Infectious Disease	Veterans Affairs Medical Center	$763,680
High Risk Infectious Disease	Virginia Tech	$1,068,111
Laser Eye Injury	Uniformed Services University of the Health Sciences	$1,599,027
Metabolically Engineered Tissue for Trauma Care	Johns Hopkins University	$340,355
Military Nutrition Research	Uniformed Services University of the Health Sciences	$1,558,944
Military Nutrition Research	University of North Dakota	$621,359
Military Relevant Disease Management	Albert Einstein College of Medicine	$2,933,914
Military Relevant Disease Management	Tripler Army Medical Center	$353,180
Military Relevant Disease Management	University of Massachusetts Medical School	$1,109,402
Military Relevant Disease Management	University of Texas Southwestern Medical Center	$1,561,796
Military Relevant Disease Management	Oregon Health and Science University	$1,902,417
Military Relevant Disease Management	Virginia Commonwealth University	$2,849,627
Military Relevant Disease Management	Thomas Jefferson University	$2,729,639
Military Relevant Disease Management	US Air Force-SG	$506,500
Military Relevant Disease Management	Naval Health Research Center	$164,494
Paget's Disease	University of Pittsburgh	*$1,045,662

Topic Area	Institution	Budget
Pre-Clinical and Clinical Activities of the Novonex/Ex-Rad Drugs	Armed Forces Radiobiology Research Institute	$1,584,656
Radiation Protection	Armed Forces Radiobiology Research Institute	$881,091
Real-Time Heart Rate Variability	Midwest Research Institute	$891,141
Sleep Management	Northeastern Ohio University College of Medicine	$640,572
Smoking Cessation	Research Triangle Institute	$2,192,298
Social Work Research	State University of New York at Stony Brook	$1,553,178
Traumatic Brain Injury	University of Florida	$2,168,431
Traumatic Brain Injury	Walter Reed Army Medical Center	$2,486,224
Traumatic Brain Injury	University of Maryland, Baltimore	$1,461,337

*Grant was funded with FY02 research dollars in the amount of $834,271.37 and FY03 research in the amount of $211,390.63

Table V: FY03 PRMRP Funding Outcomes by Topic Area and Institution

Topic Area	Institution	Budget
Acellular Matrix Research for Military Orthopedic Trauma	Baylor College of Medicine	$729,316
Alcoholism Research	Research Triangle Institute	$1,453,018
Amyotrophic Lateral Sclerosis	State University of New York, Albany	$1,152,744
Anti-diarrhea Supplement	Naval Medical Research Center	$3,704,331
Army Nutrition Research	US Army Research Institute of Environmental Medicine	$592,739
Bone-Related Disease Research	Baylor College of Medicine	$649,767
Casualty Care Research Center	Oregon Health Sciences University	$986,699
Casualty Care Research Center	Wake Forest University	$563,678
Cell Response to Anti-Cancer Agents	University of Maryland, Baltimore	$1,458,857
Epilepsy	Uniformed Services University of the Health Sciences	$1,225,862
Infectious Disease Tracking System	Foundation for Health Care Quality	$2,537,937
Interstitial Cystitis Research	University of Iowa	$973,009

Topic Area	Institution	Budget
Low Vision Research	Schepens Eye Research Institute	$2,987,463
Military Relevant Disease and Injury	University of Connecticut, Farmington	$1,732,296
Military Relevant Disease and Injury	Children's Hospital, Cincinnati	$2,562,548
Military Relevant Disease and Injury	Palomar Medical Products, Inc.	$2,499,596
Military Relevant Disease and Injury	Massachusetts General Hospital	$1,760,289
Military Relevant Disease and Injury	Naval Health Research Center	$1,041,751
Military Relevant Disease and Injury	Lovelace Respiratory Research Institute	$524,200
Military Relevant Disease and Injury	Lovelace Respiratory Research Institute	$1,828,876
Military Relevant Disease and Injury	Southern Research Institute	$1,749,271
Military Relevant Disease and Injury	Southern Research Institute	$3,987,925
Military Relevant Disease and Injury	Naval Health Research Center	$811,304
Military Relevant Disease and Injury	Naval Health Research Center	$487,270
Military Relevant Disease and Injury	Mount Sinai School of Medicine	$2,499,738
Neuroscience Research	Boston University, Boston Campus	$1,021,862
Respiratory Research	Walter Reed Army Institute of Research	$2,175,347
Smoking Cessation	San Diego State University Foundation	$134,547
Social Work Research	Research Triangle Institute	$1,435,384

Table VI: FY99-05 PRMRP Summary

	FY99	FY00	FY01	FY02	FY03	*FY04	FY05
Appropriations	$19.5M	$25M	$50M	$50M	$50M	$50M	$50M
Topic Areas Offered	15	18	31	25	28	25	23
Proposals Received	90	163	180	125	298	305	TBD**
Number of Awards	16	14	37	31	29	28	TBD**

*Award negotiations are under way

**To be determined

APPENDIX II – UNIVERSITY OF TEXAS DISEASE MANAGEMENT CENTER ANNUAL ADMINISTRATIVE REPORT

October 1, 2001 - September 30, 2003

This annual administrative report was prepared in accordance with the contract requirements outlined in the project's Scope of Work (SOW) and has been accepted by the government. This third annual report and a subsequent final supplement cover the period of October 1, 2001 through September 30, 2003. All deliverables have been received. The study has been completed successfully.

SUMMARY

The third year of the project was extremely productive and rewarding. All contractual deliverables identified in the project's SOW were accomplished. The Disease Management Center (DMC) was able to reach and exceed its projected enrollment because of a huge effort by all personnel assigned.

The third year was highlighted by many significant events in the project. Most important was the huge surge in the enrollment of patients over the past 6 months of the enrollment period. Total enrollment increased from approximately 438 patients at the beginning of the year to the end enrollment number of 1,063 patients. The final enrollment number will ensure there is enough power to provide statistically sound conclusions on the criteria being measured. Below are some key areas/issues (not all inclusive) that occurred during the third year.

Advisory Board: The project's Advisory Board (AB) continued to meet on a regularly scheduled basis. The meeting frequency was changed to a quarterly basis rather than every 2 months. The board membership was increased with the addition of a representative from William Beaumont Army Medical Center (WBAMC) in El Paso, Texas. WBAMC entered the project toward the later stage of enrollment. The AB continues as a dynamic group of individuals that provides excellent leadership, experience, and guidance to the project.

Personnel Actions: The personnel staff of the DMC remained relatively stable during this year. Personnel actions were, basically, limited to hiring personnel to fill vacancies from the departure of personnel. We continue to employ medical students on a part-time basis to assist the core staff with the tremendous workload associated with the surge in enrollment activities. Additionally, we began hiring nurses on a part-time basis to assist the DMC staff with the tremendous workload associated with the utilization review activities.

Database Development: The DMC continued to make programming upgrades to the project's primary database. Various forms were created/modified to assist with the documentation of utilization review activities. There were many additions/changes made to the various data reports providing easier ways to view needed data elements, patient enrollment, and other demographic information. The DMC also made multiple upgrades to its database that supports the logistical operations. The database was modified to provide better tracking capability of the equipment inventory. We will continue to review, modify, and/or change the databases as needed to streamline processes and better assist the staff.

Logistics: The logistics operation reached its peak workload when the enrollment concluded on March 15, 2002. A total of 278 patients was enrolled in the technology arm of the study on March 15. At this peak level of enrollment, the logistics staff was responsible for programming, packaging, and shipping approximately 45 actigraph watches per week to enrollees. In addition, the logistics staff received back from patients approximately the same number of watches that then had to have the patient data downloaded before being cleaned and prepared for the next shipment. The logistics' staff also supported patients by replacing batteries, printing paper, and defective equipment. Workload also increased in the quantity of equipment (finger pulse oximeters and blood pressure monitors) being returned by patients completing the study. All returned equipment is tested for serviceability and then returned to inventory coded as serviceable or not serviceable.

Marketing: Our marketing efforts slowed down considerably this third year. However, we were able to market and expand our boundaries west to El Paso and north to Killeen. We set up clinic/echo dates and enrolled patients in each location.

Contract Management: An amendment to the contract was received in December 2001 modifying the basic contract and approving the execution of the option period. This amendment provided for a no-cost extension to the contract that extended the contract until 1 January 2004. In addition, the option period of the contract was exercised with a start date of 1 April 2002 and a budget that was approximately $1.2M less than budgeted requirements and approximately $700,000 less than the appropriated budget. Both the original contract and the option period were being exercised concurrently effective 1 April 2002. We do have some concerns on the potential, negative impact that the budget decrement presents to the successful completion of this large research project. This concern is discussed in more detail in the Annual Administrative Budget Report submitted with this report.

Economic Analysis: The Healthcare Maintenance Model (HMM) is the analysis tool used in this project to assess and forecast utilization and cost. The design of the HMM was completed last year. All of the utilization review data that we collect will be input into the HMM to provide the utilization and cost information.

Data Safety Monitoring Board (DSMB): We continued to provide study data to the DSMB for review. The DSMB meets via conference call on a semi-annual basis.

The clinical scope of the project increased significantly during the third year. The enrollment phase of the project concluded when the last patient was enrolled on March 15, 2002 bringing the total enrollment to 1,063 participants. As mentioned earlier, we met our enrollment goal because of an aggressive final 6-month enrollment surge. At the conclusion of the enrollment period, the DMC staff has screened and/or contacted approximately 50,000 potential enrollees from about 700 cities/towns throughout south Texas. During the 6-month enrollment surge, we saw approximately 850 patients and performed approximately 900 echocardiograms. Our sonographer logged a total of 15,392 miles traveling throughout south Texas to perform echocardiograms.

Other items of interest that occurred during this year include the following:

Following the completion of the enrollment period, one of our major focuses became the collection and documentation of utilization review (UR) data on all our enrollees. Collecting and documenting the extensive UR data is a very important part of this project and a major challenge.

All the clinical personnel are involved in the UR process when they are not seeing patients in clinic. We also have hired part-time medical students and nurses to help with this huge UR tasking.

As mentioned briefly in paragraph 2.f., we expanded our study boundaries north to Darnall Army Community Hospital at Ft. Hood located just outside of Killeen, Texas and west to WBAMC at Ft. Bliss located just outside of El Paso, Texas. These two locations allowed us to use their clinical facilities to see and enroll patients from their surrounding communities. The majority of patients enrolled from these two locations are retired military or dependents.

We were able to negotiate with medical facilities in Corpus Christi and Harlingen, Texas to use their facilities to see patients. Previously, the only clinic space we had in the very southern part of Texas was located in McAllen. However, we were only allowed to use this space on Fridays and the volume of candidates in the very southern part of Texas was extensive and the demand well exceeded our 1-day per week clinic. We were able to obtain clinical space for our use up to 3 times per week in Harlingen, which is approximately 30 miles east of McAllen. This now allowed us to reach out to all the potential enrollees in the very southern part of Texas extending down to, and including, the city of Brownsville. We also were able to negotiate for the use of additional clinical space in Corpus Christi, Texas as, similar to McAllen, the potential number of enrollment candidates overwhelmed the limited clinical space we originally had in Corpus Christi. The ability to locate additional space in both Harlingen and Corpus Christi was another key factor in our ability to meet our enrollment target.

The huge numbers of potential enrollees requiring echocardiograms during the 6- month enrollment overwhelmed our capabilities. Our sonographer could perform approximately nine echocardiograms per day and the demand for echocardiograms was at least double that number. We needed to expand our echocardiogram testing or severely jeopardize our ability to meet our enrollment target. We decided to rent a second ultrasound machine and contract with two sonographers to perform echocardiograms in San Antonio while our sonographer spent much of his time traveling throughout south Texas conducting echocardiograms at many of our satellite clinics. In addition, we contracted with a diagnostic company in McAllen, Texas to perform some of our testing in that geographic area. These two initiatives enabled us to screen enough patients and end up with enough qualified candidates to meet our enrollment requirements.

The tremendous efforts of the entire DMC staff led to a very successful and productive third year of this contract. We were able to reach and exceed our enrollment goal, expand our study boundaries, and streamline processes and documentation. The DMC personnel continue to perform all their duties and responsibilities in a very professional and selfless manner. Many times these personnel were asked to take on new responsibilities and sacrifice time away from home to benefit the project. They did so without hesitation and their efforts are one of the key reasons why this third year was so productive and rewarding. We continued to stay focused and energetic as we shifted from the enrollment phase of the project to one of utilization review, data gathering, and maintaining clinical operations to see patients at their 6/12/18 anniversary dates. We look toward the next year of the project with much anticipation of the new challenges and opportunities that we will most surely encounter.

This annual administrative report is a summary of the UT DMC project during the third contractual year of operation. Any additional information or detail on this report or the DMC project can be

directed to either Jim Foley (phone: 210-567-9700 or e-mail: foleyj@uthscsa.edu) or Autumn Dawn Galbreath, MD (phone: 210-567-9700 or e-mail: galbreath@uthscsa.edu).

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APPENDIX III – DEPARTMENT OF DEFENSE HIV/AIDS PREVENTION PROGRAM (DHAPP)

Background: The African continent is currently the area of the world hardest hit by the Human Immunodeficiency Virus/Acquired Immune Deficiency Syndrome (HIV/AIDS) epidemic. Many militaries and other uniformed organizations in Africa are experiencing readiness problems resulting from high rates of HIV/AIDS among their personnel. The US Government began an initiative in FY01 to help fight the HIV/AIDS epidemic in Africa and India. The Navy was assigned as the Executive Agent for the Department of Defense (DOD) international HIV/AIDS prevention activities. The program is being managed by the Naval Health Research Center in San Diego.

Funding History: In FY01 the DOD identified $10M to begin the Program. Continued funding was provided to the DHAPP in FY02 through a $14M "congressional add" to the Defense Health Program. In FY03 funding for the Program was provided by Congress at $7M, and the language expanded the opportunity for HIV/AIDS cooperation with militaries outside of Africa. The FY04 congressional add to the Defense Health Program for Global HIV Prevention was $4.25M. In FY04 additional funding was provided to the DOD for support of militaries in selected countries through the President's Emergency Plan for AIDS Relief (PEPFAR).

Objectives of the DOD HIV/AIDS Prevention Program:

(1) Assist in developing and implementing military-specific HIV prevention programs.

(2) Integrate with, and make use of, other US Government programs and those managed by allies and the United Nations.

Implementation Strategy: The DHAPP has a bilateral and regional strategy for HIV/AIDS cooperation and security assistance. Using country priorities set by the Under Secretary of Defense (USD) for Policy, implementation of the bilateral strategy begins by coordinating with the responsible Combatant Commander and US Country Team to offer military-to-military assistance with HIV/AIDS prevention. Receptive defense forces are requested to submit an overall HIV/AIDS prevention plan to the DHAPP for evaluation. Onsite visits along with the submitted plan are used by the DHAPP to determine gaps and areas eligible for technical assistance and resource support. The DHAPP provides technical assistance and resource support to defense forces in the following areas: (1) HIV screening; (2) surveillance; (3) voluntary counseling and training; (4) peer education; (5) instructor training; (6) sexually transmitted infections syndromic management; (7) mass awareness campaigns; (8) communication and coordination; and (9) occupational exposure intervention.

Status: As of 31 December 2004, the Program is working with militaries in 41 countries around the world. Additional countries are planned for assessment in FY05. Action to resource those programs showing promise after a needs assessment has begun in 41 countries. Immediate successes have included: (1) establishing HIV/AIDS prevention programs in militaries with no prior program; (2) coordinating access of uniformed personnel to existing US Government, US Agency for International Development, and Centers for Disease Control and Prevention efforts, and host country HIV/AIDS programs; (3) providing staff in-country for HIV/AIDS prevention programs;

and (4) providing materials and consultation to develop country-specific behavioral intervention programs. The Program accomplishes these efforts mainly through direct military-to-military cooperation but limited support is provided through contracting external organizations to support specific aspects of a proposed program. In addition, a military-specific training program has been established for HIV/AIDS practitioners from militaries assisted by the Program. Trainees have begun attending this Program, and plans are being made to export the training to regional locations.

Accomplishments in FY04:

(1) Provided HIV technical assistance and resource support affecting more than 2 million uniformed personnel in 41 countries.
(2) Trained and equipped 650 military master trainers and 3,863 peer educators with military-specific HIV prevention curricula.
(3) Developed gender-specific curricula for HIV prevention education in militaries.
(4) Funded and equipped 91 voluntary counseling and testing centers on military facilities and trained 377 counselors to operate these centers. These centers tested 37,678 military personnel.
(5) Provided HIV screening and diagnostic laboratory equipment to 18 countries.
(6) Supported military-specific HIV prevention mass awareness campaigns in 27 countries.
(7) Provided 4-week long clinical training for the care and treatment of individuals infected with HIV to 50 military health care providers.
(8) Contracted 19 universities and nongovernmental organizations to support HIV prevention in militaries in Africa.

FY05 Strategy:

The Program strategy for FY05 will be characterized by the following:

(1) Continue integration with the State Department office of the Global AIDS Coordinator to expand military programs in the focus countries of the President's Emergency Plan for AIDS Relief (PEPFAR).
(2) Expand existing capability and support to militaries in sub-Saharan Africa, with approximately 65% of effort and funding directed to militaries in that part of world.
(3) Expand involvement and integration of newly established DOD Board of Directors for international HIV activities.
(4) Increase integration of the Program with US Theater Security Cooperation Plans.
(5) Further integrate partner military HIV prevention programs with local and national health programs, US Government agencies, and international HIV assistance organizations.

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